RESTRICTED ROTATION IN ARYL AMINES; RESOLUTION OF N-ALKYL-N-ACYLMESIDINES AND 5-ALKOXY-4-N-ACYL-4-ALKYLAMINO-1,3-DIMETHYLBENZENES

BY

HUGH WENDELL STEWART

B.S., University of Kentucky, 1936

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY IN THE GRADUATE SCHOOL OF THE UNIVERSITY OF ILLINOIS, 1941

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Introduction

Restricted rotation about a valence bond may lead to molecular asymmetry and to optical activity. This type of optical activity is well known in the biphenyl series. The study of restricted rotation was extended to aromatic amines by Mills and his co-workers[1,2,3,4] and later by Adams and Dankert[5] who resolved several compounds in which the only asymmetric center was restricted rotation between the amine nitrogen atom and the aromatic carbon atom to which it was attached.

The object of this research was the preparation and resolution of sterically hindered amines which have different sized groups in the *ortho* position and on the nitrogen atom, and to correlate the size of these groups with the degree of hindrance of rotation about the carbon-nitrogen valence bond.

EXPERIMENTAL AND DISCUSSION OF RESULTS

The synthesis of N-succinyl-N-ethyl-3-bromomesidine was accomplished by the following sequence of reactions: nitromesitylene to mesidine by catalytic reduction; to 3-bromomesidine by bromination of the hydrochloride; to N-ethyl-3-bromomesidine by ethylation with diethyl sulfate; to N-succinyl-N-ethyl-3-bromomesidine by acylation with succinic anhydride.

The resolution of N-succinyl-N-ethyl-3-bromomesidine was effected through the cinchonidine salt from the solvent ethyl acetate containing methanol. The less soluble salt (*l*-B, *d*-A) gave *d*-N-succinyl-N-ethyl-3-bromomesidine, $[\alpha]^{30}_{D} = +25°$ in absolute ethanol. The more soluble salt (*l*-B, *l*-A) gave *l*-N-succinyl-N-ethyl-3-bromomesidine. One of the active forms had a half life period of twenty-eight hours in

boiling *n*-butanol. The half life period of its homologue, N-succinyl-N-methyl-3-bromomesidine, as determined by Adams and Dankert[5] was nine hours.

Four of the 5-alkoxy-4-N-succinyl-4-alkylamino-1,3-dimethylbenzenes were synthesized where the alkoxy group is an ethoxy and methoxy group and the alkyl group a methyl and ethyl group. The syntheses were accomplished by the following sequence of reactions: 5-hydroxy-1,3-dimethylbenzene to 5-hydroxy-4-nitro-1,3-dimethylbenzene by nitration; to 5-alkoxy-4-nitro-1,3-dimethylbenzene by alkylation with the alkyl sulfate; to 5-alkoxy-4-amino-1,3-dimethylbenzene by catalytic reduction; to 5-alkoxy-4-alkylamino-1,3-dimethylbenzene by alkylation with dimethyl sulfate or ethyl bromide; to 5-alkoxy-4-N-succinyl-4-alkylamino-1,3-dimethylbenzene by acylation with succinic anhydride.

Resolution of 5-methoxy-4-N-succinyl-4-methylamino-1,3-dimethylbenzene (I) was effected through the cinchonidine salt from the solvent ethyl acetate containing ethanol. The less soluble salt (*l*-B, *d*-A) gave *d*-5-methoxy-4-N-succinyl-4-methylamino-1,3-dimethylbenzene, $[\alpha]^{30}_{D} = +13°$ in absolute ethanol. The more soluble salt gave *l*-5-methoxy-4-N-succinyl-4-methylamino-1,3-dimethylbenzene. Racemization of the active *d*-acid in boiling anhydrous methyl acetate (b.p. 56°) gave a half life period of 163 minutes or two and seven-tenths hours.

In the attempted resolution of the three remaining 5-alkoxy-4-N-succinyl-4-alkylamino-1,3-dimethylbenzenes prepared, no crystalline salts were obtained. The measurement of the *p*H values of ethanol-water solutions of the five acids prepared gave the same values. The measurement of the *p*H value of 2,6-dinitro-5-methoxy-4-N-succinyl-4-methylamino-1,3-dimethylbenzene (II), prepared by nitration of compound I, gave a lower *p*H value. No salts were obtained with II in its attempted resolution. It was concluded that the *p*H value of the acid plays a small part in the formation of crystalline salts.

The interference values of certain groups on a biphenyl compound have been compared with the interference values of the groups on an aryl amine. The ethyl group has been dem-

onstrated to be larger than the methyl group in its effect on restricted rotation. As in the biphenyl series the methoxy group has been demonstrated to be smaller than the methoxy group in its effect on restricted rotation.

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VITA

The writer was born in Dundee, Kentucky, on May 11, 1912. He attended a rural grade school near Owensboro, Kentucky, and graduated as Valedictorian from Daviess County High School in Owensboro, Kentucky, in May, 1930. He attended the University of Kentucky from 1930 to February, 1936, when he received the degree of Bachelor of Science in Chemistry from that institution. From that time until September, 1937, he was employed as chemist with Western Cartridge Company, East Alton, Illinois. In the fall of 1937, he entered the Graduate School of the University of Illinois, where he has continued his studies for the past four years. From June, 1938, to May, 1941, he was employed as a one-half time research chemist by the United States Regional Soybean Industrial Products Laboratory located on the campus.

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